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# Carbohydrate Counting at Meal Time Followed by a Small Secondary Postprandial Bolus Injection at 3 Hours Prevents Late Hyperglycemia, Without Hypoglycemia, After a High-Carbohydrate, High-Fat Meal in Type 1 Diabetes

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Patients with type 1 diabetes are provided guidance and structured education on adjusting their mealtime bolus insulin dose based on meal carbohydrate content. However, recent research in patients using continuous subcutaneous insulin infusion has highlighted the role of dietary fat in increasing prandial insulin requirements, particularly late into the postprandial period (1,2).

Many patients are treated with basal-bolus insulin injections, which is a less flexible method of insulin therapy than continuous subcutaneous insulin infusion, e.g., patients are unable to administer dual wave/extended bolus at mealtime. It is important to consider that patients are encouraged to count carbohydrates and administer rapid-acting insulin units at mealtime and that the time-action profiles of lispro/aspart vary in a dose-dependent manner. The peak insulin concentration after a pre-meal bolus usually occurs within the first 60 min (3), but the peak action is usually observed between 90 and 120 min, and this duration can vary between 4 and 6 h. However, peak postprandial lipemia

occurs after 3–4 h (4), which can promote acute peripheral insulin resistance and increase hepatic glucose output (5) and thus hyperglycemia.

We investigated the influence of rapid-acting insulin dose and timing after high-carbohydrate, high-fat meals in patients with type 1 diabetes using insulin analog injections.

A total of 10 male patients (mean  $\pm$  SD age  $26 \pm 4$  years, BMI  $25.4 \pm 1.6$  kg/m<sup>2</sup>, diabetes duration  $17 \pm 5$  years, age at diagnosis  $9 \pm 4$  years; HbA<sub>1c</sub>  $52.5 \pm 5.9$  mmol/mol [ $7.0 \pm 0.5\%$ ]) using insulin aspart and either basal insulin glargine ( $n = 8$ ) or detemir ( $n = 2$ ) attended the Newcastle National Institute for Health Research Clinical Research Facility at 0730 h on four occasions.

Experimental trials were randomized and involved consuming either a 1) low-fat meal with bolus insulin dictated by carbohydrate counting (Low-Fat100%), 2) high-fat meal with bolus insulin dictated by carbohydrate counting (High-Fat100%), 3) high-fat meal with a bolus insulin dose increased by 30% (High-Fat130%), or 4) high-fat meal with bolus insulin dictated by carbohydrate

counting, with an additional 30% administered at 3-h postmeal (High-FatSplit). Meals were matched for carbohydrate and protein content but differed in fat content (low fat: 68 g carbohydrate, 26 g protein, 5 g fat; high fat: 68 g carbohydrate, 26 g protein, 55 g fat). Interval blood samples were collected over a 6-h postprandial period and were processed for glucose (Biosen C-Line; EKF-Diagnostics, London, U.K.) and exogenous insulin (Invitron Insulin; Invitron, Monmouth, U.K.).

The results for glucose and insulin are presented in Fig. 1A and B, respectively. High-Fat100% was associated with late hyperglycemia, whereas 60% of patients experienced hypoglycemia (glucose  $<3.9$  mmol/L) during High-Fat130%, with no incidences under the other conditions. Postprandial glycemic excursions (time-course changes and area under the curve) were similar between Low-Fat100% and High-FatSplit, despite the additional 50 g of fat consumed in the latter trial.

When a meal has a high-carbohydrate and high-fat content using the carbohydrate counting method for insulin dose

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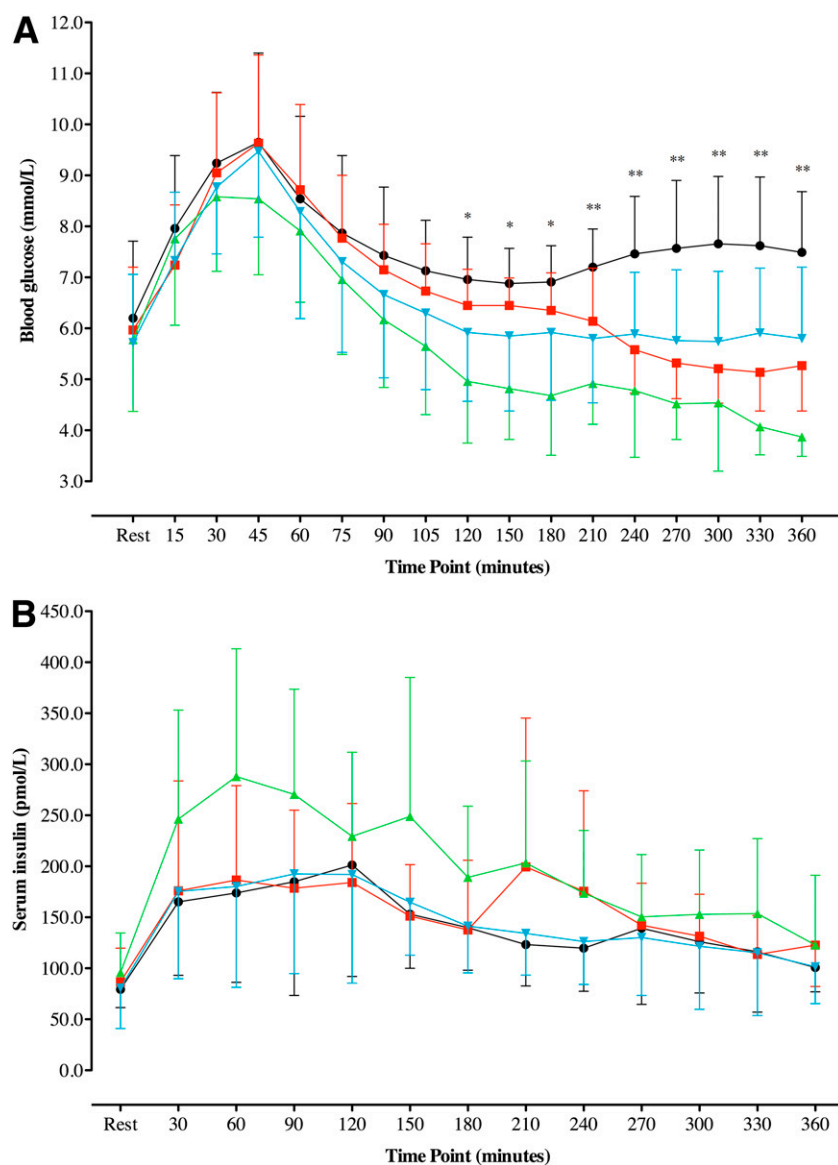
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**Figure 1**—Time-course changes in blood glucose (A) and serum insulin (B). Blue trace, Low-Fat100%; black trace, High-Fat100%; red trace, High-FatSplit; green trace, High-Fat130%. Data presented as mean  $\pm$  SD ( $n = 10$ ). \* indicates that all conditions are significantly different from High-Fat130%. \*\* indicates that all conditions are significantly different from High-Fat100% and High-Fat130%.

adjustments at mealtime and administering additional bolus insulin units 3 h later provide similar postprandial glucose control to a meal containing negligible fat,

without causing hypoglycemia. Patients should be advised that increasing the mealtime insulin dose alone is not an effective strategy and is an approach that

may increase the risk of early postprandial hypoglycemia.

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